

conservative treatment yet devised, results from its use are often disappointing.

Lateral impaction by screw-clamp or by mallet blows is not to be recommended, because such treatment almost always exaggerates the damage to the subastragaloid joint. Wrenching the heel forcibly into alignment is open to the same objection, though to a lesser degree.

Arthrodesis of the subastragaloid joint is a recently recognized treatment for such fractures. Boston orthopedic surgeons, notably Philip Wilson, have been using this operation with remarkably good results for several years.

Certainly many typical fractures lose all useful motion in the subastragaloid joint when treated by any method now in use. Crippling pain is associated with the otherwise negligible motion which remains. This pain can be cured by arthrodesis, with radical removal of exostoses from beneath the malleolus. Deforming malalignment may be corrected during the same operation.

Lateral movement at the ankle depends upon the integrity of the subastragaloid joint. Since man has come to walk nearly everywhere, upon level floors and pavements, he does not need his subastragaloid joints so much. Nevertheless, loss of this joint means a real disability, especially to workers who are constrained to stand or walk upon uneven or unstable surfaces. No joint should be needlessly sacrificed.

Some subastragaloid joints may be recovered by the traction treatment, and it is often not possible in a recent fracture to see whether or not the subastragaloid joint is too badly damaged to regain useful function. Where there is reasonable hope of recovery, primary treatment should be conservative, with the thought in mind that failure still leaves opportunity to save the day by arthrodesis.

The treatment of choice for the recent os calcis fracture with hopeless damage to the subastragaloid joint and for all other cases where a painful subastragaloid joint remains after conservative treatment is arthrodesis.

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#### Physiology, Biochemistry, and Pharmacology

### SIGNIFICANCE of Cis-Trans Isomerism in Antisepsis and Other Biological Phenomena

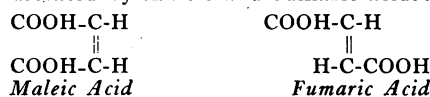
—Aside from the purely chemical differences between inorganic and organic compounds, there is a marked difference between them when the effects upon the living organism are considered. For example, arsenic is toxic in some degree regardless of its mode of chemical combination provided it can be rendered soluble and therefore absorbable. This is not the case, however, with carbon, oxygen, hydrogen, and nitrogen. The biological effects of organic substances do not depend upon the kinds of atoms constituting the molecule, but rather upon the number and arrangement of the atoms within the molecule. The formula  $C_2H_4O_2$  is the same for both acetic acid and methyl formate, but a different grouping of the atoms is responsible for the differences in their properties. The ordinary articles of food on the one hand, and substances having marked

toxic properties on the other hand may have the same ultimate composition, but they differ with respect to the numbers and positions in the molecule of the same kinds of atoms, and in their behavior toward the living organism.

The most outstanding example of the dependence of biological effects upon spatial arrangements of the atoms within the molecule is found in optical isomerism. Pasteur was the first to demonstrate the biological difference between the laevo- and dextro-rotatory forms of tartaric acid. Since then the biological importance of optical properties in organic substances has been repeatedly shown. In recent times Cushny has demonstrated their importance in the pharmacology of the atropine group. Most of the organic compounds occurring in nature are laevo-rotatory, or when both forms occur the laevo usually predominates over the dextro. In fact, life seems to be in some way intimately associated with or dependent upon laevorotation.

The type of spatial arrangement of atoms discovered by Pasteur depends upon the presence of at least one asymmetric carbon atom within the molecule, and represents only one kind of isomerism in organic compounds. There is no a priori reason for believing asymmetric carbon isomerism to be the only type of isomerism having biological significance.

The recent investigation of Cooper and Edgar<sup>1</sup> may well be the starting point of fruitful studies upon the relation of other types of isomerism to medicine, and to biology in general. These workers studied the cis-trans type of isomerism, which is well illustrated by maleic and fumaric acids:



Maleic acid represents the plane-symmetric, maleoid, or cis-form, and fumaric, the axial-symmetric, fumaroid, or trans-form.

It was shown that although maleic acid (the cis-form) was the stronger acid, fumaric acid (the trans-isomer) was the stronger germicide for a variety of organisms in vitro. The same relationship held for the methyl homologues indicating that the configuration of the molecule was a more important factor than the hydrogen-ion concentration (acidity) in determining bactericidal power. Similarly, the trans-acids exhibited a greater inhibitory effect upon the activity of the ferment diastase, a greater accelerating action upon the digestive power of pepsin, and were more efficient as protein precipitants than the cis-acids. These properties may explain the relative bactericidal action of these two isomeric forms, and also differences in their efficiency as irritants. It is of practical interest to note that although fumaric acid is said to be less toxic than maleic acid to higher animals, it is a stronger disinfectant.

The work is indeed suggestive to say the least, and it is to be hoped that the next step, namely the application of the various factors to antisepsis in vivo, will soon be undertaken. Applications in pharmacology and therapeutics also come to mind,

1. E. A. Cooper and G. H. Edgar: The Biological Significance of Cis-Trans Isomerism, *Biochem. J.*, 1926, 20:1060.

for a consideration of isomerism in its various forms may aid the further correlation of chemical structure with physiological action, and therefore give a more fundamental conception of drug action. This, it may be hoped, will materially assist in making therapeutics more rational and scientific.

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### Proctology

**T**HE treatment of hemorrhoids as indicated in current literature presents little novelty. On the whole, the prevailing opinion is that prolapsing and prolapsed hemorrhoids should be surgically removed, while others giving symptoms (mainly bleeding) may be treated with injections. The subject is fully elaborated in a recent book by J. F. Montague.<sup>1</sup> For injection he prefers, as does the writer, a 20 per cent solution of phenol in glycerine using 3-5 minims for each hemorrhoid and injecting one or two hemorrhoids at a time. Others use a 5 per cent solution of urea and quinin hydrochloride and others again 95 per cent alcohol. The hemorrhoidal masses should be made to tumefy themselves within the rim of a Kelly's proctoscope assisted by the patient endeavoring to extrude them. Each is then sharply punctured by a hypodermic needle carrying the fibrosing fluid and the necessary amount injected. There is no pain unless the fluid is injected beneath the anal mucosa, when it may be very severe. Bleeding always may be stopped by this method and mild prolapse at stool prevented. On an average four injections into each hemorrhoid will suffice to bring about shrinkage. There is no interruption in the patient's activities.

Pennington<sup>2</sup> insists on his "open" operation. A small incision is made through the mucous membrane over the everted hemorrhoid, the "varicosity protruded" and "radically removed." This method, however, does not provide for the obviously redundant mucous membrane which has become part of the prolapsing varicose mass. Apart from Pennington's method, the ligature and excision method appears that most universally accepted. The Saint Mark's Hospital, London, plan is, without divulging the sphincter, to seize each hemorrhoid, draw it downward and to incise at the ano-cutaneous margin upward for half an inch or so. The incision is in the cellular tissue and separates the mucous membrane with varicose veins internally from the sphincter externally. Braided silk is tied tightly around the upmost limit of the separated hemorrhoid, which is then cut off beyond the ligature. The ligatures slough off in a week's time. The operation takes ten minutes. There is little bleeding and the wounds are not sewn up.

New statistics are available on the occurrence of cancer in the colon. Patterson and Brown<sup>3</sup> give 91 cases in the pelvic colon and 22 and 19 in the cecum and splenic flexure respectively in a series of

171 cases. These exclude any that might possibly be thought to arise in the rectum. Walker<sup>4</sup> states that 60 per cent occur in the rectum and 20 per cent in the iliac and pelvic colon. A. H. Burgess<sup>5</sup> in 485 cases gives 46.5 per cent as occurring in the rectum and 29.4 per cent in the sigmoid colon. Seventy-five per cent of these were too extensive for radical operation, a tacit criticism of those who first see patients with colonic symptoms. In this large series 35.6 per cent were associated with acute obstruction and of these 86.7 per cent occurred in the left half of the colon. Thus "there is a 6.5 to 1 chance of a malignant growth that has caused obstruction being on the left side." The fact that more than one-third of cancers of the large bowel are associated with acute obstruction demonstrates that both in operable and inoperable cases procrastination is not permissible before an opening, either palliative or in the course of radical surgery, is made to drain the bowel above the diseased area.

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### Radiology

**R**ADIATION Therapy in Its Relation to the Cancer Problem—A well-known authority is quoted to the effect that about 10 per cent of cancer patients, excepting the skin varieties, are curable by surgery, which means that in communities where competent surgical aid is available, 10 per cent of all classes of cancer (skin cancer excepted) recover if submitted to surgery, and may be considered surgical cures. On the other hand, a classification of radiation therapy in the same analysis appears equally favorable, if not more so. Most of the radiation therapy results, on which we have reasonably reliable data, cover carcinoma of the breast and uterus. If we limit our surgical cures to these two fields the percentage would unquestionably increase, perhaps, to 15 or 20 per cent. Similarly if we limit our investigations on radiation cures to the same classification, and take statistics of such cases as are treated in acceptable institutions by x-rays and radium, the clinical cures vary from 20 to 25 per cent. In some outstanding clinics where exceptional skill in the use of radiation therapy is manifested, clinical cures run up to 30 per cent. Of course the favorable increase here is undoubtedly largely influenced by the preponderance of uterine cases over those of the breast.

Whether or not an intelligent cooperation between surgeons and radiologists, and the combined use of these agents in the field under discussion will materially increase the clinical cures, must be, in the light of experience, answered in the affirmative.

It appears that surgery, from a mechanical standpoint at least, has well-nigh reached perfection and it is difficult to visualize any drastic change from present technique either in application or results from this agency alone.

Radiation therapy, however, is still open to further study and development sufficient to warrant

1. Modern Treatment of Hemorrhoids by J. F. Montague. J. B. Lippincott, 1926.

2. Hemorrhoids, J. Rawson Pennington. J. A. M. A., December 18, 1926.

3. Cancer of the Colon, Patterson and Brown. Edin. Med. J., 1926, 33, 10.

4. Cancer of the Colon, Walker. Glasgow, Med. J., February, 1926.

5. Cancer of the Gastrointestinal Tract. A. H. Burgess, B. M. J., January 1, 1927.